

WHAT IS CLAIMED IS:

1. A method for screening for susceptibility to infection comprising:
- 5 a) obtaining sample nucleic acid from an animal; and
- b) analyzing the sample nucleic acid to detect a mutation in a gene encoding a TLR-4 polypeptide relative to a sequence of a gene encoding a native TLR-4 polypeptide;
- wherein a mutation in the gene encoding the TLR-4 polypeptide is indicative of susceptibility to infection.
- 10 2. The method of claim 1, wherein the sample nucleic acid is DNA.
3. The method of claim 1, wherein the step of analyzing the sample nucleic acid comprises sequencing the nucleic acid to obtain a sequence.
- 15 4. The method of claim 3, wherein the obtained sequence is compared to a nucleic acid sequence from a gene encoding a native TLR-4 polypeptide.
5. The method of claim 1, wherein the sequence of the gene encoding a native TLR-4 polypeptide has a nucleic acid sequence set forth in SEQ ID NO:1, SEQ ID NO:3; SEQ ID NO:5, SEQ ID NO:46, SEQ ID NO:47 or SEQ ID NO:48.
- 20 6. The method of claim 1, wherein the native TLR-4 polypeptide has an amino acid sequence set forth in of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO: 98 or SEQ ID NO:99.
- 25 7. The method of claim 1, wherein the sample nucleic acid comprises a mutation that results in a change in amino acid sequence of the encoded TLR-4 polypeptide relative to the amino acid sequence of a native TLR-4 polypeptide.
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8. The method of claim 7, wherein the sample nucleic acid comprises a mutation that results in a change from PRO to HIS at residue 712 of the native TLR-4 polypeptide amino acid sequence of SEQ ID NO:99.

9. The method of claim 7, wherein the sample nucleic acid comprises a mutation that results in a change from GLU to LYS at residue 178, a change from ARG to HIS at residue 763, a change from GLN to ARG at residue 188, a change from ASP to GLY at residue 299, a change from ASN to SER at residue 329, a change from GLU to LYS at residue 474, a change from ARG to HIS at residue 763, a change from TYR to CYS at residue 46, a change from PRO to HIS at residue 145, a change from CYS to TYR at residue 281, a change from ASN to HIS at residue 624, or a change from THR to ILE at residue 399 of the native TLR-4 polypeptide amino acid sequence of SEQ ID NO:98.

10. The method of claim 9, wherein the sample nucleic acid comprises at least a
15 second mutation.

11. The method of claim 10, wherein said second mutation results in a deletion of VAL-GLY-THR at residues 827-829 of the native TLR-4 polypeptide amino acid sequence of SEQ ID NO:98.

12. The method of claim 3, wherein the sample nucleic acid comprises at least one point mutation relative to a nucleic acid sequence from a gene encoding a native TLR-4 polypeptide.

25 13. The method of claim 12, wherein the sample nucleic acid comprises at least two point mutations relative to a nucleic acid sequence from a gene encoding a native TLR-4 polypeptide.

14. The method of claim 12, wherein said mutation is in nucleotide 2342 of the
30 nucleic acid sequence of SEQ ID NO:46.

15. The method of claim 14, wherein said at least one mutation is a change from nucleotide C to nucleotide A at position 2342 of the nucleic acid sequence.

16. The method of claim 12, wherein said at least one mutation is in Exon 2, Exon 3 or Intron 2 of the sequence of SEQ ID NO:47.

17. The method of claim 16, wherein said at least one mutation is a change from nucleotide A to nucleotide G at position 8457, a change from nucleotide G to nucleotide A at position 8612, a change from nucleotide A to nucleotide G at position 8631, a change from nucleotide A to nucleotide G at position 12245, a change from nucleotide T to nucleotide C at position 12293, a change from nucleotide C to nucleotide A at position 12412, a change from nucleotide C to nucleotide A at position 12413, a change from nucleotide A to nucleotide G at position 12541, a change from nucleotide G to nucleotide A at position 12820, a change from nucleotide A to nucleotide G at position 12874, a change from nucleotide A to nucleotide G at position 12964, a change from nucleotide C to nucleotide T at position 13174, a change from nucleotide G to nucleotide A at position 13398, a change from nucleotide G to nucleotide A at position 13769, a change from nucleotide A to nucleotide C at position 13848, a change from nucleotide G to nucleotide A at position 13937, or a change from nucleotide G to nucleotide A at position 114266 of the sequence of SEQ ID NO:47.

18. The method of claim 16, wherein said at least one mutation is a deletion of nucleotide T at position 12228 of the sequence of SEQ ID NO:47.

19. The method of claim 16, wherein said at least one mutation is a change from nucleotide A to nucleotide G at position 12245 of the gene sequence and a deletion of nucleotides 14453 to 14461 of the sequence of SEQ ID NO:47.

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20. The method of claim 16, wherein the sample nucleic acid sequence comprises at least two mutations relative to the sequence of SEQ ID NO:47.
21. The method of claim 20, wherein said at least two mutations comprise a change from nucleotide C to nucleotide T at position 12399 and a change from nucleotide G to nucleotide A at position 12510, a change from nucleotide C to nucleotide A at position 12413 and a change from nucleotide G to nucleotide A at position 14266, or a change from nucleotide A to nucleotide G at position 12874 and a change from nucleotide C to nucleotide T at position 13174 of the sequence of SEQ ID NO:47.
22. The method of claim 1, wherein the step of analyzing the sample nucleic acid comprises PCR, an RNase protection assay, or an RFLP procedure.
23. A method of reducing susceptibility of an animal to infection comprising the step of modulating an LPS mediated response in the animal.
24. The method of claim 22, further comprising the step of diagnosing an animal with an infection via analysis of a TLR-4-encoding nucleic acid sequence for a mutation relative to a sequence of a gene encoding a native TLR-4 polypeptide.
25. The method of claim 24, wherein the native TLR-4 polypeptide is a TLR-4 polypeptide that has the sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:98 or SEQ ID NO:99.
26. The method of claim 22, wherein the step of modulating LPS receptor function comprises providing a TLR-4 polypeptide to the animal.
27. The method of claim 26, wherein the TLR-4 polypeptide is a native TLR-4 polypeptide.

28. The method of claim 26, wherein the provision of a TLR-4 polypeptide is accomplished by inducing expression of a TLR-4 polypeptide.

29. The method of claim 28, wherein the expression of a TLR-4 polypeptide encoded in the animal's genome is induced.

30. The method of claim 28, wherein the expression of a TLR-4 polypeptide encoded by a nucleic acid provided to the animal is induced.

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31. The method of claim 26, wherein the provision of a TLR-4 polypeptide is accomplished by a method comprising introduction of a TLR-4-encoding nucleic acid to the animal.

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32. The method of claim 26, wherein the provision of a TLR-4 polypeptide is accomplished by injecting a TLR-4 polypeptide into the animal.

33. The method of claim 23, wherein the step of modulating LPS receptor function in the animal comprises providing a modulator of TLR-4 to the animal.

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34. The method of claim 33, wherein the modulator of TLR-4 is an agonist of TLR-4.

35. The method of claim 33, wherein the modulator of TLR-4 is an antagonist of TLR-4.

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36. The method of claim 33, wherein the modulator of TLR-4 modulates transcription of a TLR-4-encoding nucleic acid.

37. The method of claim 33, wherein the modulator of TLR-4 modulates translation of a TLR-4-encoding nucleic acid.

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39. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid
10 sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:98 or SEQ ID
NO:99.

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41. A method of modulating an LPS mediated response comprising modulating TLR-4 function in an animal.

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42. The method of claim 41, further comprising the step of diagnosing the animal for susceptibility to infection via analysis of a TLR-4-encoding nucleic acid sequence for a mutation relative to a sequence of a gene encoding a native TLR-4 polypeptide.

25 43. The method of claim 41, comprising providing a TLR-4 polypeptide to the
animal.

44.- The method of claim 43, wherein the TLR-4 polypeptide is a TLR-4 polypeptide that has the sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:98 or SEQ ID NO:99.

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45. The method of claim 43, wherein the provision of a TLR-4 polypeptide is accomplished by inducing expression of a TLR-4 polypeptide.
- 5 46. The method of claim 43, wherein the provision of a TLR-4 polypeptide is accomplished by a method comprising introduction of a TLR-4-encoding nucleic acid to the animal.
47. The method of claim 43, wherein the provision of a TLR-4 polypeptide is
10 accomplished by injecting a TLR-4 polypeptide into the animal.
48. The method of claim 41, wherein the step of modulating TLR-4 function in the animal comprises providing a modulator of TLR-4 to the animal.
- 15 49. The method of claim 48, wherein the modulator of TLR-4 is an agonist of TLR-4.
50. The method of claim 48, wherein the modulator of TLR-4 modulates transcription of a TLR-4-encoding nucleic acid.
- 20 51. The method of claim 48, wherein the modulator of TLR-4 modulates translation of a TLR-4-encoding nucleic acid.

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